Title & Detailed Synopsis of the Proposed Ph.D. Thesis

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STUDIES WITH SOME MEDICINAL PLANT-DERIVED ORGANIC MOLECULES OF BIOLOGICAL RELEVANCE

Background: For millennia, medicinal plants have been a valuable source of therapeutic agents, and still many of today's drugs are plant-derived natural products or their derivatives. However, since natural product-based drug discovery is associated with some intrinsic difficulties, pharmaceutical industry has shifted its main focus toward synthetic compound libraries and high-throughput screening (HTS) for discovery of new drug leads. The obtained results, however, did not meet the expectations as evident in a declining number of new drugs reaching the market. This circumstance revitalized the interest in natural product-based drug discovery, despite its high complexity, which in turn necessitates broad interdisciplinary research approaches.

Natural products usually refer to chemical substances produced by a living organism or found in nature possessing distinctive biological and pharmacological effects, which have played a crucial role in modern drug development and still constitute a prolific source of novel lead compounds, or pharmacophores, for ongoing drug discovery programs. Natural products are classified based upon their origins, biological functions and structures, encompassing a wide variety of chemical compound classes that include alkaloids, antibiotics, terpenoids, flavonoids, xanthonoids, phenolics, carbohydrates, lipids, proteins and amino acids, and nucleic acids. This huge diversity in chemical structures of natural products is an outcome of biosynthetic processes that have been modulated over the millennia through genetic effects. With the advent of modern techniques, particularly the rapid improvements in spectroscopic as well as accompanying advances in high-throughput screening techniques, it has become possible to have an enormous repository of bioactive natural compounds, thus opening up exciting new opportunities in the field of new drug development to the pharmaceutical industry. Medicinal chemistry of such bioactive compounds encompasses a vast area that includes their isolation and characterization from natural sources, structure modification for optimization of their activity and other physical properties, and also total and semi-synthesis for a thorough scrutiny of structure-activity relationships.

Despite substantial progresses in the fields of chemistry and biology, natural products chemistry still remains a central division of chemical and biological research with no boundaries.

Natural product chemistry may now-a-days be looked upon as a hybrid discipline! Due to the availability of huge numbers of bioactive natural products, synthetic organic chemistry, computational chemistry, medicinal chemistry, biochemistry and analytical chemistry as well as molecular biology, pharmacognosy, biotechnology, and clinical science have become the major scientific areas in the past few decades. It has been extensively demonstrated that the search for natural products, or products obtained from them through synthesis, is directed toward identifying new molecules for diseases and investigating their mechanism of actions and their specific targets of interactions (for example, DNA, RNA, Protein, and Enzymes). This fact is corroborated with the very recent literature estimating 49% of all anticancer drugs and 33% of all small molecule drugs are natural products or compounds directly derived from natural products.

Medicinal plants have thus historically been a rich source for successful drugs, and still represent an important pool for the identification of new pharmacological leads today. Renewed scientific interest in plant-derived natural product-based drug discovery is evident from the analysis of PubMed publications trends. Plants are producing numerous chemically highly diverse secondary metabolites which are optimized for exerting biological functions and are still far from being exhaustively investigated. Resulting from the revived scientific interest in natural product-based drug discovery, new approaches for the identification, characterization, and resupply of natural products are being developed, that may address some of the challenges related with the development of plant-based therapeutics. One major asset of medicinal plant-based drug discovery is the existence of ethnopharmacological information providing hints for compounds therapeutically effective in humans.

At this juncture of present-day chemical scenario, my young-mind(!) has received an encouraging stimulus to undertake a dedicated research at this spectacular filed of **plant-derived natural products**.

Objectives: The present proposal aims to undertaking phytochemical investigation of some selected indigenous medicinal plants being locally used among the tribal communities, and to studying the isolated organic molecules. The main themes of the proposed research work are as follow:

- To undertake phytochemical screening of a couple of indigenous medicinal plants such as *Cassia sophera* and *Peltophorum pterocarpum*
- Isolation, purification, and structural elucidation of the isolated phytochemicals
- Detailed spectroscopic studies of the organic molecules
- Chemical transformations with the phytochemicals in view of preparing semi-synthetic derivatives
- Quantum chemical studies of the molecules in view to investigate their molecular structures
- Single crystal X-ray properties in certain cases

Work plan: During the research tenure, the applicant plans to take up dedicated research in the prescribed field as summarized below–

- Identification and collection of plant materials
- Processing of plant materials
- Extract preparation of various plant parts
- Isolation and purification of phytochemicals from varying plant extracts
- Spectroscopic studies and structural elucidation of the isolated phytochemicals Chemical studies with the phytochemicals
- Quantum chemical studies with the phytochemicals
- X-ray studies with the phytochemicals

Methodology: Air-dried powered plant materials will be extracted with 90% ethanol in cold, and then the alcoholic extract as obtained will be concentrated under reduced pressure; the semi-solid mass then will be solvent fractionated successively with hexane, petrol ether, benzene, chloroform, ethyl acetate and water. Each fraction after making concentrated with the help of rotary evaporator will be subjected to column chromatographic resolution using pure and mixture of solvents (low polar to high polar) as eluents. Chromatographic resolution will yield solid mass that would be purified by means of further column chromatography followed by HPLC. Purified phytochemicals will then be subjected to certain chemical tests for their classification (vide ref. J. B. Harborne, Phytochemical Methods, Chapman and Hall, London, 1973, p.33-80.). Structural elucidation will be done on the basis of spectral (elemental analyses, UV, FT-IR, 1H-NMR, 13C-NMR, EIMS, 2D-NMR, HRMS) as well as chemical degradations. Detailed chemistry of each chemical constituent will cover its useful reactions, degradated products, conversion experiments. X-ray crystallographic studies of the phytochemicals will also be considered, where applicable.

Related Literature

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